

CLAIMS

What is claimed is:

1. A PTH analogue or a truncated PTH analogue or a pharmaceutically acceptable salt thereof that selectively binds to the PTH2 receptor.
2. A PTH analogue or a truncated PTH analogue or a pharmaceutically acceptable salt thereof according to claim 1 where said analogue is a selective PTH2 receptor agonist.
3. A PTH analogue or a truncated PTH analogue or a pharmaceutically acceptable salt thereof according to claim 1 where said analogue is a selective PTH2 receptor antagonist.
4. A method of selectively binding a PTH2 receptor which comprises administering to a patient in need thereof an effective amount of an analogue according to claim 1 or a pharmaceutically-acceptable salt thereof.
5. A method of selectively eliciting an agonist response from the PTH2 receptor which comprises administering to a patient in need thereof an effective amount of an analogue according to claim 2 or a pharmaceutically acceptable salt thereof.
6. A method of selectively eliciting an antagonist response from the PTH2 receptor which comprises administering to a patient in need thereof an effective amount of an analogue according to claim 3 or a pharmaceutically acceptable salt thereof.
7. An analogue according to claim 1 wherein said analogue is of formula (I),
- $$(R^1R^2)-A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-R^3,$$
- (I)
- or a pharmaceutically-acceptable salt thereof wherein
- A¹ is a hydrophilic or a lipophilic amino acid;
- A² is a lipophilic amino acid;
- A³ is a hydrophilic or a lipophilic amino acid;
- A⁴ is a hydrophilic amino acid;
- A⁵ is a hydrophilic or a lipophilic amino acid;
- A⁶ is a hydrophilic amino acid or is deleted;
- A⁷ is a hydrophilic or a lipophilic amino acid or is deleted;
- A⁸ is a lipophilic amino acid or is deleted;

(1)

R¹ and R² are each independently selected from the group consisting of H, (C₁₋₃₀)alkyl, (C₂₋₃₀)alkenyl, phenyl-(C₁₋₃₀)alkyl, naphthyl(C₁₋₃₀)alkyl, hydroxy(C₁₋₃₀)alkyl, hydroxy(C₂₋₃₀)alkenyl, hydroxy-phenyl(C₁₋₃₀)alkyl or hydroxy-naphthyl(C₁₋₃₀)alkyl;

or one of R¹ or R² is COE¹ where E¹ is (C₁₋₃₀)alkyl, (C₂₋₃₀)alkenyl, phenyl(C₁₋₃₀)alkyl, naphthyl(C₁₋₃₀)alkyl, hydroxy(C₁₋₃₀)alkyl, hydroxy(C₂₋₃₀)alkenyl, hydroxy-phenyl(C₁₋₃₀)alkyl or hydroxy-naphthyl(C₁₋₃₀)alkyl; and

R³ is OH, NH₂, (C₁₋₃₀)alkoxy or NH-Y-CH₂-Z, where Y is a (C₁₋₃₀) hydrocarbon moiety and Z is CO₂H or CONH₂;

provided that the compound is not PTH(1-34)R³, PTH(1-35)R³, PTH(1-36)R³, PTH(1-37)R³, or PTH(1-38)R³.

8. A method of selectively binding a PTH2 receptor which comprises administering to a patient in need thereof an effective amount of an analogue according to claim 7 or a pharmaceutically-acceptable salt thereof.

9. An analogue according to claim 1 of formula (II),
(R¹R²)-A¹-A²-A³-A⁴-A⁵-A⁶-A⁷-A⁸-A⁹-A¹⁰-A¹¹-A¹²-A¹³-A¹⁴-A¹⁵-A¹⁶-A¹⁷-A¹⁸-A¹⁹-A²⁰-A²¹-A²²-A²³-A²⁴-A²⁵-A²⁶-A²⁷-A²⁸-A²⁹-A³⁰-A³¹-A³²-A³³-A³⁴-A³⁵-A³⁶-A³⁷-A³⁸-R³,

(II)

or a pharmaceutically-acceptable salt thereof wherein

A¹ is Ser, Ala, Dap, Thr, Aib or is deleted;

A² is Val, Leu, Ile, Phe, Nle, β -Nal, Aib, p-X-Phe, Acc, Cha, Met or is deleted;

A³ is Ser, Thr, Aib or is deleted;

A⁴ is Glu, Asp or is deleted;

A⁵ is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe or is deleted;

A⁶ is Gln, a hydrophilic amino acid or is deleted;

A⁷ is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a lipophilic amino acid, or is deleted;

A⁸ is Met, Nva, Leu, Val, Ile, Cha, Acc, Nle, p-X-Phe, Phe, β -Nal, Bpa, a lipophilic amino acid or is deleted;

A⁹ is His, a hydrophilic amino acid or is deleted;

A¹⁰ is Asn, a hydrophilic amino acid or is deleted;

A¹¹ is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a hydrophilic amino acid or is deleted;

A¹² is Gly, Acc, Aib, or is deleted;

A¹³ is Lys, Arg or HN-CH((CH₂)_nNH-R⁴)-C(O);

A¹⁴ is His or is deleted;

A¹⁵ is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe or is deleted;

A¹⁶ is Ser, Asn, Ala, Aib or is deleted;

A¹⁷ is Ser, Thr, Aib or is deleted;

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- A^{18} is Met, Nva, Leu, Val, Ile, Nle, p-X-Phe, Phe, β -Nal, Acc, Cha, Aib or is deleted;
 A^{19} is Glu, Aib or is deleted;
 A^{20} is Arg, Lys, $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$ or is deleted;
 A^{21} is Val, Leu, Ile, Phe, Nle, β -Nal, Aib, p-X-Phe, Acc, Cha, Met or is deleted;
5 A^{22} is Acc, Aib, Glu or is deleted;
 A^{23} is Trp, Acc, Phe, p-X-Phe, Aib, β -Nal or Cha;
 A^{24} is Leu, Acc, Ile, Val, Phe, β -Nal, Nle, Aib, p-X-Phe or Cha;
 A^{25} is Arg, Lys or $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$;
 A^{26} is Arg, Lys or $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$;
10 A^{27} is Lys, Aib, Leu, hArg, Gln, Acc, Arg, Cha, Nle, Ile, Val, Phe, β -Nal, or p-X-Phe,
where the Lys is optionally substituted on the ϵ -amino group by an acyl group;
 A^{28} is Leu, Acc, Cha, Ile, Val, Phe, Nle, β -Nal, Aib or p-X-Phe;
 A^{29} is Gln, Acc or Aib;
 A^{30} is Asp, Lys, Arg or is deleted;
15 A^{31} is Val, Leu, Nle, Acc, Cha, Phe, Ile, β -Nal Aib, p-X-Phe or is deleted;
 A^{32} is His or is deleted;
 A^{33} is Asn or is deleted;
 A^{34} is Phe, Tyr, Amp, Aib, β -Nal, Cha, Nle, Leu, Ile, Acc, p-X-Phe or is deleted;
 A^{35} is Val, Leu, Nle, Acc, Cha, Phe, Ile, β -Nal Aib, p-X-Phe or is deleted;
20 A^{36} is Ala, Val, Aib, Acc, Nva, Abu or is deleted;
 A^{37} is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a lipophilic amino
acid, or is deleted;
 A^{38} is Gly, Acc, Aib, or is deleted;
25 where X for each occurrence is independently selected from the group
consisting of OH, a halo and CH_3 ;
 R^1 and R^2 are each independently selected from the group consisting of H,
 (C_{1-30}) alkyl, (C_{2-30}) alkenyl, phenyl- (C_{1-30}) alkyl, naphthyl- (C_{1-30}) alkyl,
hydroxy- (C_{1-30}) alkyl, hydroxy- (C_{2-30}) alkenyl, hydroxy-phenyl- (C_{1-30}) alkyl or
hydroxy-naphthyl- (C_{1-30}) alkyl;
30 or one of R^1 or R^2 is COE^1 where E^1 is (C_{1-30}) alkyl, (C_{2-30}) alkenyl, phenyl- (C_{1-30}) alkyl,
naphthyl- (C_{1-30}) alkyl, hydroxy- (C_{1-30}) alkyl, hydroxy- (C_{2-30}) alkenyl,
hydroxy-phenyl- (C_{1-30}) alkyl or hydroxy-naphthyl- (C_{1-30}) alkyl;
 R^3 is OH, NH_2 , (C_{1-30}) alkoxy or $\text{NH-Y-CH}_2\text{-Z}$, where Y is a (C_{1-30})
hydrocarbon moiety and Z is CO_2H or CONH_2 ;
35 n for each occurrence is independently an integer from 1 to 5; and

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R^4 for each occurrence is independently (C_1-C_{30}) alkyl, (C_1-C_{30}) acyl or $-C((NH)(NH_2))$;

provided that the compound is not PTH(1-34) R^3 , PTH(1-35) R^3 , PTH(1-36) R^3 , PTH(1-37) R^3 , or PTH(1-38) R^3 .

5 10. A compound of the formula (III),

$(R^1R^2)-A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-R^3$,

(III)

or a pharmaceutically-acceptable salt thereof wherein

10 A^1 is Ser, Ala, Dap, Thr, Aib or is deleted;

A^2 is Val, Leu, Ile, Phe, Nle, β -Nal, Aib, p-X-Phe, Acc, Cha, Met or is deleted;

A^3 is Ser, Thr, Aib or is deleted;

A^4 is Glu, Asp or is deleted;

A^5 is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe or is deleted;

15 A^6 is Gln, a hydrophilic amino acid or is deleted;

A^7 is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a lipophilic amino acid, or is deleted;

A^8 is Met, Nva, Leu, Val, Ile, Cha, Acc, Nle, p-X-Phe, Phe, β -Nal, Bpa, a lipophilic amino acid or is deleted;

20 A^9 is His, a hydrophilic amino acid or is deleted;

A^{10} is Asn, a hydrophilic amino acid or is deleted;

A^{11} is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a hydrophilic amino acid or is deleted;

A^{12} is Gly, Acc, Aib, or is deleted;

25 A^{13} is Lys, Arg or $HN-CH((CH_2)_nNH-R^4)-C(O)$;

A^{14} is His or is deleted;

A^{15} is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe or is deleted;

A^{16} is Ser, Asn, Ala, Aib or is deleted;

A^{17} is Ser, Thr, Aib or is deleted;

30 A^{18} is Met, Nva, Leu, Val, Ile, Nle, p-X-Phe, Phe, β -Nal, Acc, Cha, Aib or is deleted;

A^{19} is Glu, Aib or is deleted;

A^{20} is Arg, Lys, $HN-CH((CH_2)_nNH-R^4)-C(O)$ or is deleted;

A^{21} is Val, Leu, Ile, Phe, Nle, β -Nal, Aib, p-X-Phe, Acc, Cha, Met or is deleted;

A^{22} is Acc, Aib, Glu or is deleted;

35 A^{23} is Trp, Acc, Phe, p-X-Phe, Aib, β -Nal or Cha;

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A²⁴ is Leu, Acc, Ile, Val, Phe, β -Nal, Nle, Aib, p-X-Phe or Cha;

A²⁵ is Arg, Lys or HN-CH((CH₂)_nNH-R⁴)-C(O);

A²⁶ is Arg, Lys or HN-CH((CH₂)_nNH-R⁴)-C(O);

A²⁷ is Lys, Aib, Leu, hArg, Gln, Acc, Arg, Cha, Nle, Ile, Val, Phe, β -Nal, or p-X-Phe,

5 where the Lys is optionally substituted on the ϵ -amino group by an acyl group;

A²⁸ is Leu, Acc, Cha, Ile, Val, Phe, Nle, β -Nal, Aib or p-X-Phe;

A²⁹ is Gln, Acc or Aib;

A³⁰ is Asp, Lys, Arg or is deleted;

A³¹ is Val, Leu, Nle, Acc, Cha, Phe, Ile, β -Nal, Aib, p-X-Phe or is deleted;

10 A³² is His or is deleted;

A³³ is Asn or is deleted;

A³⁴ is Phe, Tyr, Amp, Aib, β -Nal, Cha, Nle, Leu, Ile, Acc, p-X-Phe or is deleted;

A³⁵ is Val, Leu, Nle, Acc, Cha, Phe, Ile, β -Nal, Aib, p-X-Phe or is deleted;

A³⁶ is Ala, Val, Aib, Acc, Nva, Abu or is deleted;

15 A³⁷ is Leu, Val, Nle, Ile, Cha, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, a lipophilic amino acid, or is deleted;

A³⁸ is Gly, Acc, Aib, or is deleted;

where X for each occurrence is independently selected from the group consisting of OH, a halo and CH₃;

20 R¹ and R² are each independently selected from the group consisting of H, (C₁₋₃₀)alkyl, (C₂₋₃₀)alkenyl, phenyl-(C₁₋₃₀)alkyl, naphthyl(C₁₋₃₀)alkyl, hydroxy(C₁₋₃₀)alkyl, hydroxy(C₂₋₃₀)alkenyl, hydroxy-phenyl(C₁₋₃₀)alkyl or hydroxy-naphthyl(C₁₋₃₀)alkyl;

25 or one of R¹ or R² is COE¹ where E¹ is (C₁₋₃₀)alkyl, (C₂₋₃₀)alkenyl, phenyl(C₁₋₃₀)alkyl, naphthyl(C₁₋₃₀)alkyl, hydroxy(C₁₋₃₀)alkyl, hydroxy(C₂₋₃₀)alkenyl, hydroxy-phenyl(C₁₋₃₀)alkyl or hydroxy-naphthyl(C₁₋₃₀)alkyl;

R³ is OH, NH₂, (C₁₋₃₀)alkoxy or NH-Y-CH₂-Z, where Y is a (C₁₋₃₀) hydrocarbon moiety and Z is CO₂H or CONH₂;

n for each occurrence is independently an integer from 1 to 5; and

30 R⁴ for each occurrence is independently (C₁-C₃₀)alkyl, (C₁-C₃₀)acyl or -C((NH)(NH₂));

provided that when A⁸ is not a lipophilic D-amino acid or is not deleted then at least one of A⁶, A⁷, A⁹, A¹⁰, A¹¹ and A¹² is a D-amino acid or at least one of A⁶, A⁷, A⁹, A¹⁰, A¹¹, A¹², A¹³, A¹⁴, A¹⁵, A¹⁶, A¹⁷, A¹⁸, A¹⁹, A²⁰, A²¹ and A²² is deleted;

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and further provided that when the compound contains a D-amino acid then A³⁶ is deleted.

11. A compound according to claim 10 wherein said compound is

- [D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
5 [D-Nle⁸]hPTH(1-34)NH₂,
[D-Leu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Cha⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Phe⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Nal⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
10 [D-Abu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Met⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Met⁸]hPTH(1-34)NH₂,
[D-Ile⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Ile⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
15 [D-Ile⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Leu⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Leu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Val⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Val⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
20 [D-Val⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Cha⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Cha⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Ala⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Ala⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
25 [D-Ala⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Phe⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Phe⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Nal⁸]hPTH(1-34)NH₂,
[D-Trp⁸]hPTH(1-34)NH₂,
30 [Cha^{7, 11}, D-Trp⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Trp⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Abu⁸]hPTH(1-34)NH₂,
[Cha^{7, 11}, D-Abu⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
[D-Nle⁸, Nle¹⁸]hPTH(1-34)NH₂,
35 [des-Met⁸]hPTH(1-34)NH₂,

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- [Cha^{7,11}, des-Met⁸]hPTH(1-34)NH₂,
 [Cha^{7,11}, des-Met⁸, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Met⁸, des-Met¹⁸]hPTH(1-34)NH₂,
 [Cha^{7,11}, des-Met⁸, des-Met¹⁸]hPTH(1-34)NH₂,
 5 [des-Met⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Met¹⁸]hPTH(1-34)NH₂,
 [Cha^{7,11}, des-Met¹⁸]hPTH(1-34)NH₂,
 [Cha^{7,11}, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [D-Nle⁸, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 10 [des-Glu⁶, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Leu⁷, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-His⁹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Asn¹⁰, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Leu¹¹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 15 [des-Gly¹², Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Lys¹³, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-His¹⁴, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Leu¹⁵, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Asn¹⁶, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 20 [des-Ser¹⁷, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Glu¹⁹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Arg²⁰, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Val²¹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Glu²², Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 25 [des-Glu⁶, Cha^{7,11}, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Leu⁷, Nle^{8,18}, Cha¹¹, Tyr³⁴]hPTH(1-34)NH₂,
 [Cha^{7,11}, des-His⁹, Nle^{8,18}, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Glu⁶, Cha^{7,11}, D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [des-Leu⁷, D-Nle⁸, Cha¹¹, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 30 [Cha^{7,11}, D-Nle⁸, des-His⁹, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [Cha^{7,11}, D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-31)NH₂,
 [Cha^{7,11}, des-Met⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [Cha^{7,11}, D-Nle⁸, des-Met¹⁸, Tyr³⁴]hPTH(1-34)NH₂,
 [Cha^{7,11}, des-Met⁸, des-His⁹, des-Asn¹⁰]hPTH(1-34)NH₂,
 35 [Cha^{7,11}, des-Ser¹⁷, des-Met¹⁸, des-Glu¹⁹]hPTH(1-34)NH₂,

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[D-Met⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂,

[D-Met⁸, Tyr³⁴]hPTH(1-34)NH₂,

[D-Bpa⁸, Tyr³⁴]hPTH(1-34)NH₂,

[D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(7-34)NH₂,

5 [D-Nle⁸, Nle¹⁸]hPTH(7-34)NH₂ or

[D-Met⁸]hPTH(7-34)NH₂.

12. A compound according to claim 11 wherein said compound is

[Cha^{7,11}, des-Met⁸, Nle¹⁸, Tyr³⁴]hPTH-(1-34)NH₂,

[Cha^{7,11}, D-Nle⁸, des-Met¹⁸, Tyr³⁴]hPTH-(1-34)NH₂,

10 [Cha^{7,11}, D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH-(1-34)NH₂,

[D-Nle⁸, Nle¹⁸, Tyr³⁴]hPTH(1-34)NH₂ or [D-Bpa⁸, Tyr³⁴]hPTH(1-34)NH₂.

13. A PTHrP analogue of formula (IV) that selectively binds to the PTH2 receptor,

(R¹R²)-A¹-A²-A³-A⁴-A⁵-A⁶-A⁷-A⁸-A⁹-A¹⁰-A¹¹-A¹²-A¹³-A¹⁴-A¹⁵-A¹⁶-A¹⁷-A¹⁸-A¹⁹-A²⁰-A²¹-A²²-A²³-

15 A²⁴-A²⁵-A²⁶-A²⁷-A²⁸-A²⁹-A³⁰-A³¹-A³²-A³³-A³⁴-A³⁵-A³⁶-A³⁷-A³⁸-R³,

(IV)

or a pharmaceutically acceptable salt thereof, wherein

A¹ is Ala, Ser, Dap, Thr, Aib or is deleted;

A² is Val or is deleted;

20 A³ is Ser, Aib, Thr or is deleted;

A⁴ is Glu, Asp or is deleted;

A⁵ is His, Ile, Acc, Val, Nle, Phe, Leu, p-X-Phe, β -Nal, Aib, Cha or is deleted;

A⁶ is Gln, a hydrophilic amino acid or is deleted;

A⁷ is Leu, Val, Cha, Nle, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, Aib, a lipophilic amino acid or is deleted;

A⁸ is Leu, Met, Acc, Cha, Aib, Nle, Phe, Ile, Val, β -Nal, p-X-Phe, a lipophilic amino acid or is deleted;

A⁹ is His, a hydrophilic amino acid or is deleted;

A¹⁰ is Asp, Asn, a hydrophilic amino acid or is deleted;

30 A¹¹ is Lys, Arg, Leu, Cha, Aib, p-X-Phe, Ile, Val, Nle, Acc, Phe, β -Nal, HN-CH((CH₂)_nNH-R⁴)-C(O), a lipophilic D-amino acid, a hydrophilic amino acid or is deleted;

A¹² is Gly, Acc, Aib or is deleted;

A¹³ is Lys, Arg, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

35 A¹⁴ is Ser, His or is deleted;

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- A^{15} is Ile, Acc, Cha, Leu, Phe, Nle, β -Nal, Trp, p-X-Phe, Val, Aib or is deleted;
 A^{16} is Gln, Aib or is deleted;
 A^{17} is Asp, Aib or is deleted;
 A^{18} is Leu, Aib, Acc, Cha, Phe, Ile, Nle, β -Nal, Val, p-X-Phe or is deleted;
5 A^{19} is Arg, Lys, Aib, $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$ or is deleted;
 A^{20} is Arg, Lys, $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$ or is deleted;
 A^{21} is Arg, Lys, $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$ or is deleted;
 A^{22} is Phe, Glu, Aib, Acc, p-X-Phe, β -Nal, Val, Leu, Ile, Nle or Cha;
 A^{23} is Phe, Leu, Lys, Acc, Cha, β -Nal, Aib, Nle, Ile, p-X-Phe, Val or Trp;
10 A^{24} is Leu, Lys, Acc, Nle, Ile, Val, Phe, β -Nal, Aib, p-X-Phe, Arg or Cha;
 A^{25} is His, Lys, Aib, Acc, Arg or Glu;
 A^{26} is His, Aib, Acc, Arg or Lys;
 A^{27} is Leu, Lys, Acc, Arg, Ile, Val, Phe, Aib, Nle, β -Nal, p-X-Phe or Cha;
 A^{28} is Ile, Leu, Lys, Acc, Cha, Val, Phe, p-X-Phe, Nle, β -Nal, Aib or is deleted;
15 A^{29} is Ala, Glu, Acc, Aib or is deleted;
 A^{30} is Glu, Leu, Nle, Cha, Aib, Acc, Lys, Arg or is deleted;
 A^{31} is Ile, Leu, Cha, Lys, Acc, Phe, Val, Nle, β -Nal, Arg or is deleted;
 A^{32} is His or is deleted;
 A^{33} is Thr, Ser or is deleted;
20 A^{34} is Ala, Phe, Tyr, Cha, Val, Ile, Leu, Nle, β -Nal, Aib, Acc or is deleted;
 A^{35} is Glu, Asp or is deleted;
 A^{36} is Ile, Acc, Cha, Leu, Phe, Nle, β -Nal, Trp, p-X-Phe, Val, Aib or is deleted;
 A^{37} is Arg, Lys, $\text{HN-CH}((\text{CH}_2)_n\text{NH-R}^4)\text{-C(O)}$ or is deleted;
 A^{38} is Ala, Phe, Tyr, Cha, Val, Ile, Leu, Nle, β -Nal, Aib, Acc or is deleted;
25 R^1 and R^2 are each independently selected from the group consisting of H,
 (C_{1-30}) alkyl, (C_{2-30}) alkenyl, phenyl- (C_{1-30}) alkyl, naphthyl- (C_{1-30}) alkyl,
hydroxy- (C_{1-30}) alkyl, hydroxy- (C_{2-30}) alkenyl, hydroxy-phenyl- (C_{1-30}) alkyl or
hydroxy-naphthyl- (C_{1-30}) alkyl;
or one of R^1 or R^2 is COE^1 where E^1 is (C_{1-30}) alkyl, (C_{2-30}) alkenyl, phenyl- (C_{1-30}) alkyl,
30 naphthyl- (C_{1-30}) alkyl, hydroxy- (C_{1-30}) alkyl, hydroxy- (C_{2-30}) alkenyl,
hydroxy-phenyl- (C_{1-30}) alkyl or hydroxy-naphthyl- (C_{1-30}) alkyl;
 R^3 is OH, NH_2 , (C_{1-30}) alkoxy or $\text{NH-Y-CH}_2\text{-Z}$, where Y is a (C_{1-30})
hydrocarbon moiety and Z is CO_2H or CONH_2 ;
n for each occurrence is independently an integer from 1 to 5; and

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R^4 for each occurrence is independently (C_1-C_{30}) alkyl, (C_1-C_{30}) acyl or $-C((NH)(NH_2))$;

provided that the compound is not PTHrP(1-34) R^3 , PTHrP(1-35) R^3 , PTHrP(1-36) R^3 , PTHrP(1-37) R^3 or PTHrP(1-38) R^3 ,

5 and further provided that the compound is not [Ile⁵, Trp²³]PTHrP(1-36) or [Trp²³]PTHrP(1-36).

14 A compound of formula (V),

$(R^1R^2)-A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-R^3$,

10 (V)

or a pharmaceutically acceptable salt thereof, wherein

A^1 is Ala, Ser, Dap, Thr, Aib or is deleted;

A^2 is Val or is deleted;

A^3 is Ser, Aib, Thr or is deleted;

15 A^4 is Glu, Asp or is deleted;

A^5 is His, Ile, Acc, Val, Nle, Phe, Leu, p-X-Phe, β -Nal, Aib, Cha or is deleted;

A^6 is Gln, a hydrophilic amino acid or is deleted;

A^7 is Leu, Val, Cha, Nle, β -Nal, Trp, Pal, Acc, Phe, p-X-Phe, Aib, a lipophilic amino acid or is deleted;

20 A^8 is Leu, Met, Acc, Cha, Aib, Nle, Phe, Ile, Val, β -Nal, p-X-Phe, a lipophilic amino acid or is deleted;

A^9 is His, a hydrophilic amino acid or is deleted;

A^{10} is Asp, Asn, a hydrophilic amino acid or is deleted;

A^{11} is Lys, Arg, Leu, Cha, Aib, p-X-Phe, Ile, Val, Nle, Acc, Phe, β -Nal, HN-

25 $CH((CH_2)_nNH-R^4)-C(O)$, a lipophilic D-amino acid, a hydrophilic amino acid or is deleted;

A^{12} is Gly, Acc, Aib or is deleted;

A^{13} is Lys, Arg, HN- $CH((CH_2)_nNH-R^4)-C(O)$ or is deleted;

A^{14} is Ser, His or is deleted;

30 A^{15} is Ile, Acc, Cha, Leu, Phe, Nle, β -Nal, Trp, p-X-Phe, Val, Aib or is deleted;

A^{16} is Gln, Aib or is deleted;

A^{17} is Asp, Aib or is deleted;

A^{18} is Leu, Aib, Acc, Cha, Phe, Ile, Nle, β -Nal, Val, p-X-Phe or is deleted;

A^{19} is Arg, Lys, Aib, HN- $CH((CH_2)_nNH-R^4)-C(O)$ or is deleted;

35 A^{20} is Arg, Lys, HN- $CH((CH_2)_nNH-R^4)-C(O)$ or is deleted;

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A²¹ is Arg, Lys, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A²² is Phe, Glu, Aib, Acc, p-X-Phe, β-Nal, Val, Leu, Ile, Nle or Cha;

A²³ is Phe, Leu, Lys, Acc, Cha, β-Nal, Aib, Nle, Ile, p-X-Phe, Val or Trp;

A²⁴ is Leu, Lys, Acc, Nle, Ile, Val, Phe, β-Nal, Aib, p-X-Phe, Arg or Cha;

5 A²⁵ is His, Lys, Aib, Acc, Arg or Glu;

A²⁶ is His, Aib, Acc, Arg or Lys;

A²⁷ is Leu, Lys, Acc, Arg, Ile, Val, Phe, Aib, Nle, β-Nal, p-X-Phe or Cha;

A²⁸ is Ile, Leu, Lys, Acc, Cha, Val, Phe, p-X-Phe, Nle, β-Nal, Aib or is deleted;

A²⁹ is Ala, Glu, Acc, Aib or is deleted;

10 A³⁰ is Glu, Leu, Nle, Cha, Aib, Acc, Lys, Arg or is deleted;

A³¹ is Ile, Leu, Cha, Lys, Acc, Phe, Val, Nle, β-Nal, Arg or is deleted;

A³² is His or is deleted;

A³³ is Thr, Ser or is deleted;

A³⁴ is Ala, Phe, Tyr, Cha, Val, Ile, Leu, Nle, β-Nal, Aib, Acc or is deleted;

15 A³⁵ is Glu, Asp or is deleted;

A³⁶ is Ile, Acc, Cha, Leu, Phe, Nle, β-Nal, Trp, p-X-Phe, Val, Aib or is deleted;

A³⁷ is Arg, Lys, HN-CH((CH₂)_nNH-R⁴)-C(O) or is deleted;

A³⁸ is Ala, Phe, Tyr, Cha, Val, Ile, Leu, Nle, β-Nal, Aib, Acc or is deleted;

20 R¹ and R² are each independently selected from the group consisting of H, (C₁₋₃₀)alkyl, (C₂₋₃₀)alkenyl, phenyl-(C₁₋₃₀)alkyl, naphthyl(C₁₋₃₀)alkyl, hydroxy(C₁₋₃₀)alkyl, hydroxy(C₂₋₃₀)alkenyl, hydroxy-phenyl(C₁₋₃₀)alkyl or hydroxy-naphthyl(C₁₋₃₀)alkyl;

25 or one of R¹ or R² is COE¹ where E¹ is (C₁₋₃₀)alkyl, (C₂₋₃₀)alkenyl, phenyl(C₁₋₃₀)alkyl, naphthyl(C₁₋₃₀)alkyl, hydroxy(C₁₋₃₀)alkyl, hydroxy(C₂₋₃₀)alkenyl, hydroxy-phenyl(C₁₋₃₀)alkyl or hydroxy-naphthyl(C₁₋₃₀)alkyl;

30 R³ is OH, NH₂, (C₁₋₃₀)alkoxy or NH-Y-CH₂-Z, where Y is a (C₁₋₃₀) hydrocarbon moiety and Z is CO₂H or CONH₂;

n for each occurrence is independently an integer from 1 to 5; and

35 R⁴ for each occurrence is independently (C₁-C₃₀)alkyl, (C₁-C₃₀)acyl or -C((NH)(NH₂));

provided that when A⁸ is not a lipophilic D-amino acid or is not deleted then at least one of A⁶, A⁷, A⁹, A¹⁰, A¹¹ and A¹² is a D-amino acid or at least one of A⁶, A⁷, A⁹, A¹⁰, A¹¹, A¹², A¹³, A¹⁴, A¹⁵, A¹⁶, A¹⁷, A¹⁸, A¹⁹, A²⁰, A²¹ and A²² is deleted.

15. A compound according to claim 14 wherein said compound is
35 [Ile⁵, D-Leu⁸]hPTHrP(1-34)NH₂.

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- [Ile⁵, D-Leu⁸, Trp²³]hPTHrP(1-34)NH₂,
 [Ile⁵, des-Leu⁸, Trp²³]hPTHrP(1-34)NH₂,
 [Ile⁵, des-Leu⁸]hPTHrP(1-34)NH₂,
 [des-Leu⁸, Trp²³]hPTHrP(1-34)NH₂,
 5 [Ile⁵, des-Leu¹⁸]hPTHrP(1-34)NH₂,
 [Ile⁵, des-Leu¹⁸, Trp²³]hPTHrP(1-34)NH₂,
 [des-Leu¹⁸, Trp²³]hPTHrP(1-34)NH₂,
 [Ile⁵, D-Leu⁸, Glu^{22,25}, Leu^{23,28,31}, Lys^{26,30}, Aib²⁹]hPTHrP(1-34)NH₂,
 [Ile⁵, D-Leu⁸, Glu^{22,25}, Trp²³, Lys^{26,30}, Leu^{28,31}, Aib²⁹]hPTHrP(1-34)NH₂,
 10 [Ile⁵, D-Leu⁸, Glu^{22,25,29}, Leu^{23,28,31}, Lys^{26,30}]hPTHrP(1-34)NH₂,
 [Ile⁵, D-Leu⁸, Glu^{22,25,29}, Trp²³, Lys^{26,30}, Leu^{28,31}]hPTHrP(1-34)NH₂ or
 [D-Leu⁸, Trp²³]hPTHrP(7-34)NH₂.

16. A method of selectively binding the PTH2 receptor which comprises administering to a patient in need thereof an analogue according to claim 9 or a
 15 pharmaceutically acceptable salt thereof.

17. A method of selectively binding the PTH2 receptor which comprises administering to a patient in need thereof a compound according to claim 10 or a pharmaceutically acceptable salt thereof.

18. A method of selectively binding the PTH2 receptor which comprises
 20 administering to a patient in need thereof a compound according to claim 11 or a pharmaceutically acceptable salt thereof.

19. A method of selectively binding a PTH2 receptor which comprises administering to a patient in need thereof a compound according to claim 12 or a pharmaceutically acceptable salt thereof.

20. A method of selectively binding a PTH2 receptor which comprises administering to a patient in need thereof an analogue according to claim 13 or a pharmaceutically acceptable salt thereof.

21. A method of selectively binding a PTH2 receptor which comprises administering to a patient in need thereof a compound according to claim 14 or a
 30 pharmaceutically acceptable salt thereof.

22. A method of selectively binding a PTH2 receptor which comprises administering to a patient in need thereof a compound according to claim 15 or a pharmaceutically acceptable salt thereof.

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23. A pharmaceutical composition comprising an analogue according to claim 9 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

24. A pharmaceutical composition comprising a compound according to claim 10 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

25. A pharmaceutical composition comprising a compound according to claim 11 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

26. A pharmaceutical composition comprising a compound according to claim 12 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

27. A pharmaceutical composition comprising an analogue according to claim 13 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

28. A pharmaceutical composition comprising a compound according to claim 14 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

29. A pharmaceutical composition comprising a compound according to claim 15 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

30. A method of treating a medical disorder that results from altered or excessive action of the PTH2 receptor, which comprises administering to a patient in need thereof an effective amount of an analogue according to claim 7, sufficient to inhibit the activation of the PTH2 receptor of said patient.

31. A method of treating a medical disorder that results from altered or excessive action of the PTH2 receptor, which comprises administering to a patient in need thereof an effective amount of an analogue according to claim 9, sufficient to inhibit the activation of the PTH2 receptor of said patient.

32. A method of treating a medical disorder that results from altered or excessive action of the PTH2 receptor, which comprises administering to a patient in need thereof an effective amount of a compound according to claim 10, sufficient to inhibit the activation of the PTH2 receptor of said patient.

33. A method of treating a medical disorder that results from altered or excessive action of the PTH2 receptor, which comprises administering to a patient in

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41. A method according to claim 33 wherein said medical disorder is abnormal CNS functions, abnormal pancreatic functions, divergence from normal mineral metabolism and homeostasis, male infertility, abnormal blood pressure or a hypothalamic disease.

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42. A method according to claim 34 wherein said medical disorder is abnormal CNS functions, abnormal pancreatic functions, divergence from normal mineral metabolism and homeostasis, male infertility, abnormal blood pressure or a hypothalamic disease.

5 43. A method according to claim 35 wherein said medical disorder is abnormal CNS functions, abnormal pancreatic functions, divergence from normal mineral metabolism and homeostasis, male infertility, abnormal blood pressure or a hypothalamic disease.

10 44. A method according to claim 36 wherein said medical disorder is abnormal CNS functions, abnormal pancreatic functions, divergence from normal mineral metabolism and homeostasis, male infertility, abnormal blood pressure or a hypothalamic disease.

15 45. A method according to claim 37 wherein said medical disorder is abnormal CNS functions, abnormal pancreatic functions, divergence from normal mineral metabolism and homeostasis, male infertility, abnormal blood pressure or a hypothalamic disease.

20 46. A method of treating a medical disorder that results from altered or excessive action of the PTH2 receptor, which comprises administering to a patient in need thereof an effective amount of a PTH analogue or a truncated PTH analogue or a pharmaceutically acceptable salt thereof according to claim 1, sufficient to inhibit the activation of the PTH2 receptor of said patient.

25 47. A method according to claim 46 wherein said medical disorder is abnormal CNS functions, abnormal pancreatic functions, divergence from normal mineral metabolism and homeostasis, male infertility, abnormal blood pressure or a hypothalamic disease.

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